

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Klinksiek, et al.
Serial No. : 10/679,123
Filed : October 3, 2003
For : PROCESS FOR PRODUCING PULVURENT ACTIVE
SUBSTANCE FORMULATIONS WITH COMPRESSIBLE
FLUIDS
Art Unit : 1615
Examiner : Snigdha Maewall

Hon. Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR 1.131

Sir:

We, the undersigned, citizens of Germany, hereby declare as follows:

1. We are the joint inventors of the subject matter disclosed and claimed in the above-identified application.
2. At a time prior to July 11, 2002, we conceived of the invention disclosed and claimed in the above-identified application.
3. At a time prior to July 11, 2002, we actually reduced the invention to practice by preparing the disclosed pulverulent active substance by the claimed process, as evidenced by the attached page from our invention record, together with an English translation.

4. Between the time of the conception, and the actual reduction to practice, we worked diligently to prepare the disclosed pulverulent active substance by the claimed process.

5. That prior to July 11, 2002, we contacted our patent attorney in Germany, and sent him an email with copies of our laboratory notebook pages and an invention disclosure attached. A copy of that email, with copies of the attachments and English translations of the same, are attached hereto.

6. From a time prior to July 11, 2002, up until the filing date of our German Priority Application on October 18, 2002 we worked diligently with our patent attorney in Germany to prepare the patent application for filing.

We declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date

2010-03-12

Inventor

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LeA 36130

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Erfindungsmeldung

Ort, Datum

Leverkusen, 2002-05-03

Für Arbeitnehmer der Bayer AG ist RP Patente und Lizenzen für die Entgegennahme von Erfindungsmeldungen zuständig.

Bezeichnung

(Kurze, schlagwortartige Kennzeichnung zur Charakterisierung)

Verfahren zur Herstellung pulverförmiger Wirkstoffformulierungen mit kompressiblen Fluiden

1. Angaben zur Erfindung

1.1 Technische Aufgabe

(Kurze Angabe über technische Problemstellung, die Ausgang für die gemeldete Lösung war)

Konventionelle Formulierungen schwerlöslicher Wirkstoffe mit akzeptabler Wirkung lassen sich nur mit unbefriedigend niedrigen Wirkstoffkonzentrationen herstellen. Neu Ansätze zur Überwindung der Problematik basieren auf dem Einsatz überkritischer Medien. Aufgabe war es, den Stand der Technik dieser Verfahren aufzuarbeiten und auszutesten.

1.2 Lösung

(Kurze Darstellung der Lösung der unter 1.1 geschilderten technischen Aufgabe, die als schutzfähige Erfindung angesehen wird)

Stabile, amorphe Nanopartikelformulierungen von Wirkstoffen lassen sich durch Schmelzdispersion von Wirkstoffsuspensionen in Gegenwart von geeigneten Emulgatoren, anschließende physikalische Verkapselung durch filmbildende Polymere und (Sprüh-)Trocknung herstellen. Die erhaltenden Pulver oder Granulate lassen sich wie wasserdispersierbare Pulver oder wasserdispersierbare Granulate anwenden. Nachteil dieses Verfahrens ist, dass der Wirkstoff aufgeschmolzen werden muß. Thermolabile Wirkstoffe lassen sich auf diese Weise nicht verarbeiten. Es wurde gefunden, dass durch den Zusatz von überkritischem CO₂ die Dispersion zu feinteiligen Partikeln deutlich unterhalb des Schmelzpunktes gelingt.

1.3 Stand der Technik

(Vollständige Angaben über den Ihres Wissens nächstliegenden Stand der Technik/Literaturstellen und deren Relevanz. (Gegebenenfalls Beiblatt benutzen)

LeA 35177: Schmelzdispersion mit erreichbarer Wirkstoffteilchengröße < 1 µm mit Nachteil s.o.

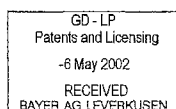
PGSS (WO95/21688): Mikronisierung des Wirkstoffes durch Explosionswirkung des überkritischen Mediums beim Entspannen. Teilchengröße ca. 10 µm.

1.4 Beigefügte Unterlagen

(In der Regel Anmeldungsentwurf, Beispiele, Zeichnungen)

Patententwurf vom 2002-04-11

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To
Bayer AG
LP - Patents and Licensing
51368 Leverkusen
Bldg.: Q 18

internal reference:

Dr. Bramer-Weger

BW

Le A 36130

(for completion by LP Patents and Licensing)

Notification of Invention

Place, Date

Leverkusen, 2002-05-03

For Bayer AG employees, LP Patents and Licensing is responsible for accepting notifications of invention

Title

(Brief identification on key word basis for characterization)

Process for producing pulverulent active substance formulations with compressible fluids

1. Details of the invention

1.1 Technical problem

(Brief statement of technical problem on which the notified solution was based)

Conventional formulations of low-solubility active substances with acceptable effect can only be produced with unsatisfactorily low active substance concentrations. New approaches at overcoming these problems are based on the use of supercritical media. The problem was to develop and test the state of the art in these processes.

1.2 Solution

(Brief description of the solution to the technical problem outlined in 1.1, considered to be a patentable invention)

Stable, amorphous nanoparticle formulations of active substances can be produced by melt dispersing of active substance suspensions in the presence of suitable emulsifiers, subsequent physical encapsulation by film-forming polymers, and (spray) drying. The resultant powders or granules can be used in the same way as water-dispersible powders or water-dispersible granules. A disadvantage of this process is that the active substance has to be melted. Active substances that are

not heat-stable cannot be processed in this way. It has been found that, through the addition of supercritical CO₂, dispersion to form finely divided particles can be successfully accomplished at well below the melting point.

1.3 Prior art

(Full details on what you consider to be the closest prior art/literature references and their relevance) (Use extra sheet if needed)

LeA 35177: melt dispersing with attainable active substance particle size < 1 µm with disadvantage as above.

PGSS (WO95/21688): micronization of the active substance through the explosion effect of the supercritical medium on pressure release. Particle size about 10 µm.

1.4 Appended documents

(Usually draft application, examples, drawings)

Patent draft dated 2002-04-11